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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **SYSTEMS AND METHODS FOR BIOPOLYMER ENGINEERING**

(57) Abstract: Methods, computer systems, and computer program products for biopolymer engineering. A variant set for a biopolymer of interest is constructed by identifying, using a plurality of rules, a plurality of positions in the biopolymer of interest and, for each respective position in the plurality of positions, substitutions for the respective position. The plurality of positions and the substitutions for each respective position in the plurality of positions collectively define a biopolymer sequence space. A variant set comprising a plurality of variants of the biopolymer of interest is selected. A property of all or a portion of the variants in the variant set is measured. A sequence-activity relationship is modeled between (i) one or more substitutions at one or more positions of the biopolymer of interest represented by the variant set and (ii) the property measured for all or the portion of the variants in the variant set. The variant set is redefined to comprise variants that include substitutions in the plurality of positions that are selected based on a function of the sequence-activity relationship.

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<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC(7) : G01N33/00, 48 US CL : 702/19,27 According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) U.S. : 702/19,27 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Schneider G. Peptide design by artificial neural networks and computer-based evolutionary search. Biochemistry, October 13, 1998, Vol. 95, Issue 21, 12179-12184	1-54
X	US 2002/0177170 (LUO et al) 11/28/2002	1-54
X	US 20020119492 A1 (CHIRINO et al), August 29, 2002	1-54
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents:		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E"	earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed	
Date of the actual completion of the international search 02 December 2005 (02.12.2005)		Date of mailing of the international search report 24 FEB 2006
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201		Authorized officer Michael Born Telephone No. ((571) 272-054

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International application No.

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## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-54

- Remark on Protest**
- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
  - ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
  - ☒ No protest accompanied the payment of additional search fees.

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### BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

Group I, claims 1-54, drawn to method for constructing set of variants of biopolymer.

Group II, claims 59,65, drawn to variant set, or components thereof, obtained according to claim 1 or 6.

Group III, claims 58,64, drawn to nucleic acids encoding variants obtained according to claim 1 or 6.

Group IV, claims 66,67,72,73, drawn to cells containing variants obtained according to claim 1 or 6 or containing polynucleotides encoding therefor.

Group V, claims 55-57,61, drawn to variant set, or components thereof, obtained according to claim 2.

Group VI, claim 60, drawn to nucleic acids encoding variants obtained according to claim 2.

Group VII, claims 68,69, drawn to cells containing variants obtained according to claim 2 or containing polynucleotides encoding therefor.

Group VIII, claims 63, drawn to variant set, or components thereof, obtained according to claim 4.

Group IX, claim 62, drawn to nucleic acids encoding variants obtained according to claim 4.

Group X, claims 70,71, drawn to cells containing variants obtained according to claim 4 or containing polynucleotides encoding therefor.

Group XI, claims 74-89, drawn to method of weighting selection rules.

Group XII, claims 91,97, drawn to to variant set, or components thereof, obtained according to claims 75,88.

Group XIII, claims 90,96, drawn to nucleic acids encoding variants obtained according to claims 75,88.

Group XIV, claim 92, drawn to to variant set, or components thereof, obtained according to claims 84.

Group XV, claim 93, drawn to nucleic acids encoding variants obtained according to claims 84.

Group XVI, claim 94, drawn to to variant set, or components thereof, obtained according to claims 86.

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Group XVII, claim 95, drawn to nucleic acids encoding variants obtained according to claims 86.

Group XVIII, claims 98-115, drawn to computer software.

Group XIX, claim 116, drawn to computer system.

The inventions listed as Groups I-XIX do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Groups directed to "variants" is the technical feature that links Groups I to XIX. The claims of the Groups directed to variants are not the contribution over the prior art because they are suggested by references teaching any sets of substituted biopolymers, e.g., sets of substituted polypeptides. For example, such sets of peptides are taught in US 6,423,686 directed to substituted LHRH derivatives. Therefore, the lack of unity is present because the linking technical feature is not a "special technical feature" as defined by PCT Rule 13.2. Further, the variants of Groups II, V, VIII are not addressed as having common core structure, and are clearly distinct as their structure satisfies different functional requirements. Same for groups directed to corresponding nucleic acids or cells.